

CHAPTER 5

RISK CHARACTERIZATION

5.1 QUANTITATIVE RISK EVALUATION

5.1.1 RISK CALCULATIONS

In contrast to calculation of average lifetime dose for the oral and inhalation routes of exposure, which is based on an administered dose, the evaluation of exposure for the dermal route is based on an estimated absorbed dose, or dermal absorbed dose (DAD). The DAD term is calculated separately for the water and soil pathways, as described in Chapter 3. In Chapter 4, the oral toxicity values are adjusted according to the estimated extent of gastrointestinal absorption in critical toxicity studies. Once the DAD and the adjusted toxicity values have been derived, the cancer risk and hazard index for the dermal route are calculated using Equations 5.1 and 5.2. For evaluating the risk, the age-adjusted child/adult receptor is the most sensitive receptor for cancer endpoints. For non-cancer endpoints, the child is the most sensitive receptor.

The steps involved in the dermal risk assessment are summarized in Exhibit 5-1.

5.1.2 RISKS FOR ALL ROUTES OF EXPOSURE

Endpoints for assessment of risk for the

dermal pathway are based on induction of systemic toxicity and carcinogenesis, as they are for the oral and the inhalation routes of exposure. Therefore, the estimate of total risk for exposure to either soil or water contaminants is based on the summation of individual risks for the oral, the inhalation, and the dermal routes.

5.2 UNCERTAINTY ASSESSMENT

The importance of adequately characterizing uncertainty in the risk assessment is emphasized in several U.S. EPA documents (U.S. EPA, 1992b; U.S. EPA, 1995a; U.S. EPA, 1997a; U.S. EPA, 1997b). EPA's 1995 Policy for Risk Characterization calls for greater clarity, transparency, reasonableness and consistency in Agency risk assessments. To ensure transparency and clarity, the Workgroup recommends that an assessment of the confidence, uncertainties, and influence of these uncertainties on the outcome of the risk assessment be presented.

Several sources of uncertainty exist in the recommended approach for estimating exposure and risks from dermal contact with water and soil. Many of these uncertainties are identified in the *DEA*, Chapter 10. Exposure parameters with highly variable distributions are likely to have a greater impact on the outcome of the risk assessment than those with lower variability. Which exposure parameters will vary the

Calculation of Dermal Cancer Risk

$$\text{Dermal cancer risk} = \text{DAD} \times \text{SF}_{\text{ABS}} \quad (5.1)$$

where:

<u>Parameter</u>	<u>Definition (units)</u>	<u>Default Value</u>
DAD	= Dermal Absorbed Dose (mg/kg-day)	See Equation 3.1 or Exhibit B-3 (water) See Equations 3.11 and 3.12 (soil)
SF _{ABS}	= Absorbed cancer slope factor (mg/kg-day) ⁻¹	See Equation 4.2

Calculation of Dermal Hazard Quotient

$$\text{Dermal hazard quotient} = \frac{DAD}{RfD_{ABS}} \quad (5.2)$$

where:

Parameter	Definition (units)	Default Value
DAD	= Dermal Absorbed Dose (mg/kg-day)	See Equation 3.1 or Exhibit B.3 (water) See Equations 3.11 and 3.12 (soil)
RfD _{ABS}	= Absorbed reference dose (mg/kg-day)	See Equation 4.3

EXHIBIT 5-1

SUMMARY OF DERMAL RISK ASSESSMENT PROCESS

Risk Assessment Process		Cancer Risk		Hazard Index	
Hazard ID		Section 2		Section 2	
Exposure Assessment	Child or Adult	Water Dose	Soil Dose	Water Dose	Soil Dose
		Section 3.1, Equations 3.1-3.4	Section 3.2, Equations 3.11/3.12	Section 3.1, Equations 3.1-3.4	Section 3.2, Equations 3.11/3.12
	Age-adjusted Child/Adult SFS _{ADJ}	See Note	Section 3.2.2.5, Equation 3.21	See Note	Section 3.2.2.5, Equation 3.21
Toxicity Assessment		Section 4, SF _{ABS} , Equation 4.2		Section 4, RfD _{ABS} , Equation 4.3	
Risk Characterization		Section 5.1, Equation 5.1 DAD x SF _{ABS}		Section 5.1, Equation 5.2 DAD/RfD _{ABS}	
		Uncertainty Analysis Section 5.2			

Note: The calculations used in developing the screening tables in Appendix B (Exhibits B-3 and B-4) for the water pathway determined that the adult receptor experiences the highest dermal dose. Therefore, the adult exposure scenario is recommended for screening purposes. However, if an age-adjusted exposure scenario for the dermal route is selected to be consistent with methods for determining the risk of other routes of exposure (e.g. oral), sample calculations are provided in Appendix D as guidance.

most will depend on the receptor, (i.e., residential adult, commercial adult, adolescent trespasser) and chemical evaluated. For the dermal-soil pathway, the adherence factor and the value used to represent the concentration in soil are likely to be sensitive variables regardless of the receptor. For the dermal-water pathway, the K_p and the value used to represent the

concentration in water are likely to be sensitive variables.

A detailed analysis of the uncertainty associated with every exposure model and exposure variable presented in this guidance is not possible due to insufficient data. RAGS Part E recommends that a qualitative evaluation of key exposure variables and

models, and their impact on the outcome of the assessment, be conducted when the database does not support a quantitative Uncertainty Analysis. Below is a discussion of key uncertainty issues associated with the recommended approach for dermal risk assessments in this guidance. Exhibit 5-2 summarizes

which contribute 10% or more of the dose that is achieved through the drinking water pathway. Although this is a reasonable assumption for exposure assessments in which the drinking water pathway is evaluated, this may result in a slight underestimate of the overall exposure and risk. In addition, the selection

EXHIBIT 5-2

SUMMARY OF UNCERTAINTIES ASSOCIATED WITH DERMAL EXPOSURE ASSESSMENT

Exposure Factor	High	Medium	Low
COPC selection for dermal-water pathway			X
C_w - exposure point concentration	site-specific, data-dependent		
C_w - ionization state			X
Event duration for showering (t_{event})			X
K_p	X		
C_{soil} - exposure point concentration	site-specific, data-dependent		
Event time for dermal-soil pathway		X	
Surface area (SA) - dermal-soil pathway		X	
Exposure frequency (EF)		X	
Adherence Factor (AF)	X		
Default dermal-soil absorption values and lack of absorption values for other compounds (ABS_d)		X	
Lack of dermal slope factor for cPAHs and other compounds	X		
Lack of info on GI absorption (ABS_{GI})		X	

the degree of uncertainty associated with the dermal exposure assessment.

5.2.1 HAZARD IDENTIFICATION

Uncertainty is associated with the assumption that the only chemicals of concern in the risk assessment for the dermal-water pathway are those

of chemicals of concern for the dermal-soil pathway is limited by the availability of dermal absorption values for soil. If soil dermal absorption values are not available, a chemical may be dropped out of the quantitative evaluation of risk, which could potentially result in an underestimate of risk. The recommended default screening value of 10% for semivolatile organic

chemicals should limit the degree of underestimation associated with this step of the dermal risk assessment approach.

5.2.2 EXPOSURE ASSESSMENT

5.2.2.1 Dermal Exposure to Water – Uncertainties Associated with the Model for DA_{event}

When evaluating uncertainties, it is important to keep in mind that the model used to estimate exposure can contribute significantly to uncertainty. Uncertainty in model predictions arises from a number of sources, including specification of the problem, formulation of the conceptual model, interpretation, and documentation of the results. Although some attempts have been made to validate the model for DA_{event} utilized in this document, a greater effort and more formal process will be necessary before a more accurate assessment of the sources of uncertainty associated with the model can occur. A detailed discussion of the model for DA_{event} , its validation and remaining uncertainties is presented in Appendix A, Sections A.1.4 and A.3.

Concentration in water (C_w). The value used for C_w in the equation for DA_{event} is dependent on several factors, including the method for estimating the exposure point concentration (EPC) (e.g., 95% upper confidence limit of the mean [95%UCL], a maximum concentration, etc.); and the physico-chemical characteristics of the water-borne chemicals. The Superfund program advocates the use of the 95%UCL in estimating exposure to contaminants in environmental media. This policy is based on the assumption that individuals are randomly exposed to chemicals in soil, water, sediment, etc., in a given exposure area and that the arithmetic mean best represents this exposure. To develop a conservative estimate of the mean, a 95% UCL is adopted. However, when data are insufficient to estimate the 95%UCL, any value used for C_w (whether it be a 95%UCL, maximum value or arithmetic mean) is likely

to contribute significantly to the uncertainty in estimates of the DA_{event} . The degree to which the value chosen for the EPC contributes to an over- or under-estimate of exposure depends on the representativeness of existing data and the estimator used to represent the EPC.

The bioavailability of a chemical in water is dependent on the ionization state of that chemical, with the non-ionized forms more readily available than the ionized forms. To be most accurate in estimating the dermally absorbed dose, the DA_{event} should be equal to the sum of the DA_{event} values for the non-ionized and ionized species (see Section 3.1.2.2). For most Superfund risk assessments, however, the DA_{event} is most likely to be based on a C_w which is derived directly from a laboratory report. The value presented in a laboratory report represents the total concentration of ionized and non-ionized species and thus does not provide the information necessary to calculate separate DA_{event} values for ionized and non-ionized groups. A slight overestimate of exposure for organic chemicals of low molecular weight is likely to occur if the equations presented in Section 3.1.2.1 are not utilized.

Another factor affecting bioavailability of chemicals in water is the aqueous solubility of the chemical and adsorption to particulate material. Although filtration of water samples in the field has been used to reduce turbidity and estimate the soluble fraction of chemicals in water, the use of data from filtered samples is not recommended for either ingestion or dermal exposure assessments. Therefore, data from unfiltered samples should be used as the basis for estimating the chemical concentration (C_w) for calculating the dermal dose. The use of data from unfiltered samples may tend to overestimate the concentration of chemical that is available for absorption, the extent of the overestimate determined

by the magnitude of the difference between the filtered and unfiltered sample. However, water sample collection methods should be employed that minimize turbidity, rather than relying on sample filtration. The impact of this health-protective assumption can be discussed in the Uncertainty Analysis.

In addition, since the concentration of some compounds in water decreases greatly during showering, the impact of volatilization should be considered when estimating C_w for the dermal-water pathway. The exposure analysis for the inhalation pathway should account for compounds which volatilize.

Exposure Time. The recommended default assumptions for exposure time in showering/bathing scenarios are 15 minutes for the central tendency scenario and 35 minutes for the RME scenario. This is consistent with the recommended 50th and 95th percentiles for showering presented in EPA's *EFH*. If a showering/bathing scenario exceeded 35 minutes (the recommended central tendency and RME exposure parameters for bathing time are 20 and 60 minutes, respectively), the default assumption for exposure time might result in a slight underestimate of risk. The degree of underestimation is dependent on the actual showering time.

Permeability coefficients (K_p). Permeability coefficients have been identified as major parameters contributing uncertainty to the assessment of dermal exposure for contaminants in aqueous media (*DEA*). Two major groups of uncertainties can be identified. The Flynn database, upon which the predictive K_p correlation is derived, includes *in vitro* data for approximately 90 compounds. The log K_{ow} and MW of these compounds and the experiments designed to measure their K_p values introduce some measures of uncertainty into the correlation coefficients. Using this correlation to predict K_p introduces several other uncertainties. Accuracy of K_{ow} (whether measured or estimated) would affect both the correlation coefficient of Equation 3.8 and the predicted K_p of specific

chemicals. Different interlaboratory experimental conditions (e.g., skin sample characteristics, temperature, flow-through or static diffusion cells, concentration of chemicals in solution) influence the value of the resulting measured K_p included in the Flynn database.

Since the variability between the predicted and measured K_p values is no greater than the variability in interlaboratory replicated measurements, this guidance recommends the use of predicted K_p for all organic chemicals. This approach will ensure consistency between Agency risk assessments in estimating the dermally absorbed dose from water exposures. The Flynn database contains mostly smaller hydrocarbons and pharmaceutical drugs which might bear little resemblance to the typical compounds detected at Superfund sites. Predicting K_p from this correlation is uncertain for highly lipophilic and halogenated chemicals with log K_{ow} and MW which are very high or low as compared to compounds in the Flynn database, as well as for those chemicals which are partially or completely ionized. Alternative approaches are recommended for the highly lipophilic and halogenated chemicals, which attempt to reduce the uncertainty in their predicted K_p values.

Another major source of uncertainty comes from the use of K_p obtained from *in vitro* studies to estimate (*in vivo*) dermal exposure at Superfund sites. This could introduce further uncertainty in the use of estimated K_p in the assessment of exposure and risk from the dermal-water pathway.

5.2.2.2 Dermal Exposure to Soil

Concentration in soil (C_{soil}). The Superfund program advocates the use of the 95% UCL in estimating exposure to contaminants in environmental media. This policy is based on the assumption that individuals are randomly exposed to chemicals in soil, water, sediment, etc., in a given exposure area and that the arithmetic mean best represents this exposure.

To develop a conservative estimate of the mean, a 95% UCL is adopted. However, when there are

insufficient data to estimate the 95% UCL, any value used for C_{soil} (whether it be a 95% UCL, maximum value or arithmetic mean) is likely to contribute significantly to the uncertainty in estimates of the DA_{event} . The degree to which the value chosen for the EPC contributes to an over- or under-estimate of the exposure is dependent on the representativeness of the existing data and the estimator used to represent the EPC.

Event time (EV). In order to be consistent with assumptions about absorption, the equation for DAD presented in this guidance assumes (by default) that the event time is 24 hours, (i.e., that no washing occurs and the soil remains on the skin for 24 hours). This assumption probably overestimates the actual exposure time for most site-specific exposure scenarios and is likely to result in an overestimate of exposure. The degree to which exposure could be overestimated is difficult to determine without information on absorption rates for each chemical.

Surface area and frequency of exposure. Default adherence values recommended in this guidance are weighted by the surface area exposed and are based on the assumption that adults will be wearing short sleeved shirts, shorts and shoes and that a child will be wearing a short-sleeved shirt, shorts and no shoes. This may not match the year-round exposure scenario assumed to exist at every site. For instance, there is a four-fold difference between the surface area exposed for a residential adult based on the default assumption of clothing worn versus an assumption that an adult is wearing a long-sleeved shirt, and long pants. There is also a four-fold difference between the surface area exposed of a residential child based on the default assumption of clothing worn versus an assumption that a child is wearing a long-sleeved shirt, long pants, shoes and socks. The value chosen for surface area can introduce a moderate degree of uncertainty into exposure and risk estimates. Risk assessors may need to adjust defaults depending upon site conditions such as climate and activity patterns.

The value chosen for frequency can also introduce moderate amounts of uncertainty into

exposure and risk assessment estimates. For instance, it is assumed that a resident comes into contact with residential soils 350 days/yr. If the actual frequency is significantly less (for instance one day per week, equivalent to 52 days/yr), a seven-fold difference occurs, which directly impacts exposure and risk estimates.

Adherence factors. Although RAGS Part E provides dermal adherence factors for several different types of receptors, the conditions at a particular site may not match the conditions in the study upon which the default dermal adherence factor is based, (i.e., specific activity, clothing worn, soil type, soil moisture content, exposure duration, etc). For example, Kissel, *et al.* (1996), has found that finer particles adhere preferentially to the hands unless soils are greater than 10% moisture. Some studies have found that soil particles greater than 250 microns do not adhere readily to skin. Thus the soil type, including moisture content, can affect the adherence of soil. In addition, the specific activity which occurs in the site-specific exposure scenario may not directly match the activities for which adherence factors are available in this guidance. All of these factors can introduce significant uncertainties into the exposure assessment. Each of these factors should be carefully evaluated in each risk assessment conducted for the dermal pathway.

Dermal-soil absorption factors. The amount of chemical absorbed from soil is dependent on a number of chemical, physical and biological factors of both the soil and the receptor. Examples of factors in soil which can influence the amount of chemical that is available to be absorbed include; soil type, organic carbon content, cation exchange capacity, particle size, temperature, pH, etc. For example, increasing particle size has been found to correspond with decreased absorption across the skin for some chemicals. Chemical factors which can affect absorption include lipid solubility, chemical speciation, aging of the chemical, etc. Physical factors which can impact absorption include soil loading rate, surface area exposed to soil, soil contact time and soil adherence. For example, fraction absorbed from soil is dependent on the soil loading. In general, as the soil loading

increases, the fraction absorbed should be constant, until one gets above a critical level at which the skin surface is uniformly covered by soil (i.e., the mono-layer). Since nearly all existing experimental determinations of fraction absorbed have been conducted above the mono-layer, the actual fraction absorbed could be larger than experimentally determined. Biological factors which can affect absorption include diffusivity of skin, skin blood flow, age of the receptor, etc. The exact relationship of all of these factors to dermal absorption is not known. Thus, there is uncertainty in the default dermal absorption factors. This discussion should be presented in the risk assessment, but until more is understood quantitatively about this effect, adjustment of the dermal-soil absorption factors is not warranted.

Default Dermal Absorption Values for Semivolatile Organic Chemicals. This guidance identifies a default dermal absorption value of 10% for semivolatile organic compounds as a class. This suggested value is based on the assumption that the observed experimental values presented in Exhibit 3-4 are representative of all semivolatile organic compounds for which measured dermal-soil absorption values do not exist. Chemicals within classes vary widely in structure and chemical properties. The use of default dermal absorption values based on chemical class can introduce uncertainties into the risk assessment which can either over- or under-estimate the risk.

Lack of dermal-soil absorption values. The ability to quantify the absorption of contaminants from exposure to soil is limited. Chemical-specific information is available for only a few chemicals. For most chemicals, no data are available, so dermal exposures have not been quantified. This lack of data results in the potential underestimation of total exposure and risk. The degree of the underestimation is dependent on the chemical being evaluated.

5.2.3 TOXICITY ASSESSMENT

Oral reference doses and slope factors for dermal exposures. Quantitative toxicity estimates for dermal exposures have not been developed by EPA. Therefore, oral reference doses and oral cancer potency factors are used to assess systemic toxicity from dermal exposures. The dermal route of exposure can result in different patterns of distribution, metabolism, and excretion than occur from the oral route. When oral toxicity values for systemic effects are applied to dermal exposures, uncertainty in the risk assessment is introduced because these differences are not taken into account. Since any differences between oral and dermal pathways would depend on the specific chemical, use of oral toxicity factors can result in the over- or underestimation of risk, depending on the chemical. It is not possible to make a general statement about the direction or magnitude of this uncertainty.

Lack of a dermal slope factor for polynuclear aromatic hydrocarbons (PAHs) and other chemicals. This guidance focuses on the expected systemic effects of dermal exposure from chemicals in soil and water. EPA does not have recommended toxicity values for the adverse effects that can occur at the skin surface. This lack of dermal toxicity values is considered to be a significant gap in the evaluation of the dermal pathway, particularly for carcinogenic PAHs. The statement in RAGS claiming that “it is inappropriate to use the oral slope factor to evaluate the risks associated with exposure to carcinogens such as benzo(a)pyrene, which causes skin cancer through direct action at the point of application” should not be interpreted to mean that the systemic effects from exposure to dermally active chemicals should not be evaluated. In fact, there is a significant body of evidence in the literature to generate a dose-response relationship for the carcinogenic effects of PAHs on the skin. In addition, PAHs have also been shown to induce systemic toxicity and tumors at distant organs. For these reasons, the lack of dermal toxicity values may significantly underestimate the risk to exposure to PAHs and potentially other compounds in soil. Until dermal dose-response factors are developed, EPA recommends that a quantitative evaluation be

conducted for systemic effects of PAHs and other compounds and that a qualitative evaluation be conducted for the carcinogenic effects of PAHs and other compounds on the skin.

5.2.4 RISK CHARACTERIZATION

Lack of information for GI absorption. One issue in the dermal-soil risk assessment approach presented in this guidance is how would the route comparison (i.e., oral to dermal) change if the GI tract absorption fraction were much less than the assumed 100%. As discussed in Chapter 10 of the *DEA*, cancer slope factors are intended to be used with administered dose. Since dermal doses are absorbed, it is necessary

to convert the SF to an absorbed basis which can be done in an approximate way by dividing it by the GI tract absorption fraction. When ABS_{GI} is high, adjustment of the SF to an absorbed dose is not as important and the earlier conclusions for when the dermal dose exceeds the ingested dose do not change. However, when ABS_{GI} is low, the adjustment of the SF to an absorbed dose can substantially increase the importance of the dermal route relative to the ingestion route and it is important to consider. In the absence of information on gastrointestinal absorption, the risk characterization for the dermal pathway has used unadjusted reference doses and slope factors. This may result in underestimation of risk for dermal exposures to both soil and water.